Drug pipeline: Q312

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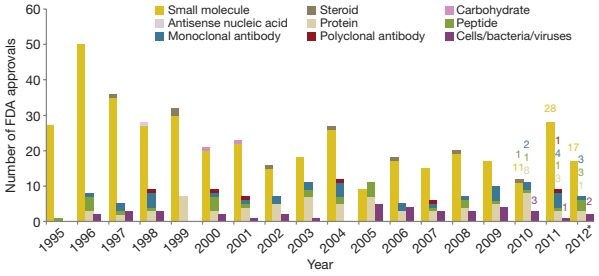
The long-awaited thumbs-up for a gene therapy finally came through, with the November approval by the EMA of Glybera (alipogene tiparvovec) for patients lacking lipoprotein lipase. Other notable approvals are Aubagio (teraflunomide), the second small-molecule drug for multiple sclerosis, and Kyprolis (carfilzomib), an irreversible proteasome inhibitor for multiple myeloma. Some drugs addressing unmet oncology needs (pancreatic and mesothelioma) are showing positive signs in trials, and the first systemic antisense drug, Kynamro (mipomersen sodium), will be going before the FDA shortly.

FDA approvals by drug molecule type



Source: US Food and Drug Administration; BioMedTracker, of service a Sagient Research (http://www.biomedtracker.com/).
*Partial year 1/1/12 to 10/10/12.

Notable setbacks (Q3 2012)

Drug/company	Indication	Setback summary
IB1001 (trenonacog alpha/Ipsen	Hemophilia B	7/10/12. FDA put clinical hold on two phase 3 trials due to unusually high levels of antibodies to Chinese hamster proteins
ABT-384/Abbott	Mild to moderate Alzheimer's disease	7/19/12. Company suspended development of this small-molecule inhibitor of 11-beta hydroxysteroid dehydrogenase due to failure to improve symptoms
IDX184/Idenix	Hepatitis C	8/16/12. FDA put a partial hold on phase 2 trial due to cardiac events encountered with competitor's product (nucleotide polymerase inhibitors
IDX19368/Idenix	Hepatitis C	8/27/12. FDA put a partial hold on phase 2 trial due to cardiac events encountered with competitor's product (nucleotide polymerase inhibitors
LY2140023 (pomaglumetad methionil)/Lilly	Schizophrenia	8/29/12. Company suspended phase 3 trial of peptide prodrug of the mGlu2/3 agonist due to independent analysis showing it unlikely to be positive
Talactoferrin/ Agennix	Non–small cell lung cancer	8/6/12. Company announced that phase 3 trial of targeted dendritic cell recruiter and activator did not improve survival compared to placebo
Tanezumab/ Pfizer	Arthritis pain	9/9/12. Company announced results of phase 3 trial showing no difference between treatment with monoclonal antibody against nerve growth factor and placebo
Vatreptacog alpha/ Novo Nordisk	Hemophilia A,B clotting problems	9/28/12. Company discontinued development due to the production of anti-drug antibodies in phase 3 trial

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/).

Notable clinical trial results (Q3 2012)

Drug/company	Indication	Summary
Bavituximab/Peregrine	Pancreatic cancer	Phase 2 results of anti-phosphatidyl serine mAb in combination with gemcitabine showed four patients with partial response (AACR 6/20/12)
LY-2409021/Lilly	Diabetes mellitus, type II	Phase 2 results with this glucagon antagonist showed reduction in HbA1c compared to placebo (American Diabetes Association, Abstract 981-P, 6/09/2012)
Amatuximab/Esai	Mesothelioma	Phase 2 results of 89 patients showed 39% with partial response, 51% with stable disease (*J.Clin.Oncol.* **30**, 2012 (suppl.; abstr. 7030))
Alisertib/Takeda	Breast cancer	Second-generation aurora kinase inhibitor in phase 2 trial with taxene-based chemotherapy showed partial responses in eight patients, three with stable disease (ASCO 6/1/12)
AUY922/Novartis	Breast cancer	Phase 2b study of HSP9 inhibitor for safety and efficacy showed few adverse effects and 23% partial responses (ASCO, Abstract 530, 6/2/2012)
BAY 86-9766 /Bayer	Hepatocellular cancer	Phase 2 study of MEK inhibitor with sorafenib showed 5% partial response, 38% stable disease (ASCO, Abstract 4103, 6/4/2012)
LDE225/Novartis	Brain cancer (malignant glioma; AA and GBM)	Phase 2 study of Smoothened antagonist from hedgehog pathway showed 2/33 patients with complete response, both with hedgehog positive tumors (ASCO, Abstract 9519, 6/4/2012)
Trastuzumab emtansine (TDM-1)/Roche	Breast cancer	Phase 2 results of conjugated mAB showed 54% with partial response, no significant cardiotoxicity (ASCO, Abstract 532, 6/2/2012)
Afatinib/Boehringer Ingelheim	Non–small cell lung cancer	Phase 3 trial of dual kinase (HER-2, EGFR) inhibitor showed median survivial times longer in patients with EGFR and KRAS mutations (European Society for Medical Oncology, Abstract 1339, 9/28/2012)

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). FDA, US Food and Drug Administration; EMA, European Medicines Agency.

Notable regulatory approvals (Q3 2012)

Product/company	Indication	Drug Information
Kyprolis (carfilzomib)/ Onyx	Multiple myeloma	7/12/12, FDA. tetrapeptide epoxyketone irreversibly binds 20S proteasome
Zaltrap (aflibercept)/ Regeneron	Colorectal cancer	8/12/12, FDA. anti-angiogenesis fusion protein that binds VEGF-A, VEGF-B and placental growth factor
TevaGrastim (Tbo-filgrastim)/Teva	Neutropenia/leukopenia	8/12/12, FDA. G-CSF, biosimilar of Neupogen
Linzess (linaclotide acetate)/Ironwood	Chronic idiopathic constipation/irritable bowl syndrome	8/12/12, FDA. first-in-class agonist of intestinal guanylate cyclase c receptor
Xtandi (enzalutamide)/ Astellas	Prostate cancer	8/12/12, FDA. androgen receptor antagonist, blocks nuclear translocation of androgen receptor, DNA binding and coactivator recruitment
Tretten (catridecacog)/ Novo Nordisk	Factor XIII deficiency	9/3/12, EMA. recombinant Factor XIII
Gattex (teduglutide)/ NPS Pharmaceuticals	Short bowel syndrome	9/4/12, EMA. glucagon-like peptide-2 analog
Aubagio (teriflunomide)/ Sanofi	Multiple sclerosis	9/12/12, FDA. oral immunomodulating agent blocks dihydroorate dehydrogenase and pyrimidine biosynthesis, reducing immune cell proliferation
Fycompa (perampanel)/ Eisai	Partial seizures (epilepsy)	10/12/12, FDA. first-in-class selective noncompetitive antagonist of AMPA receptor for glutamate
Synribo (omacetaxine mepesuffinate)/Teva	Chronic myelogenous leukemia (CML)	10/12/12, FDA. small-molecule inhibitor of protein synthesis, first for CML
Jetrea (ocriplasmin)/ ThromboGenics	Vitreomacular adhesion	10/17/12, FDA. recombinant microplasmin, a truncated stable form of plasmin
Glybera (alipogene tiparvovec)/uniQure	Lipoprotein lipase deficiency	11/02/12, EMA. first gene therapy in the West; lipoprotein lipase packed in adeno-associated virus, administered through intramuscular injections
Xeljanz/tofacitinib/Pfizer	Rheumatoid arthritis	11/06/12, FDA. pan-JAK inhibitor is the first of its kind for an autoimmune disorder

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). FDA, US Food and Drug Administration; EMA, European Medicines Agency; VEGF, vascular endothelial growth factor; G-CSF, granulocyte colony-stimulating factor; JAK, Janus kinase inhibitor.

Notable upcoming regulatory decisions (Q1 2013)

Drug/company	Indication	Upcoming catalyst
Budesonide MMX/ Santarus	Ulcerative colitis	1/16/13, PDUFA. Budesonide is a steroid inserted in a three-component matrix comprising successive amphiphilic, lipophilic/inert matrices (carnauba wax, stearic acid) dispersed in hydrophilic matrices (diethylene glycol monoethyl ether); delivered to colon, reducing pre-colon absorption
Kynamro (mipomersen sodium)/Sanofi	Dyslipidemia/hypercholesterolemia	1/29/13, PDUFA. Mipomersen sodium is a 20-mer phosphorothioate antisense oligonucleotide that is complementary to human apolipoprotein B-100 (apoB-100) mRNA
Ampligen/ Hemispherx	Chronic fatigue syndrome	2/1/13, PDUFA. poly I:poly C12U, a specific form of mismatched double-stranded ribonucleic acid (dsRNA)
Heplisav/Dynavax	Hepatitis B virus (HBV) vaccine	2/24/13, PDUFA. Heplisav is an intramuscular hepatitis B virus vaccine comprising a toll-like receptor (TLR)-9 agonistic immunostimulatory sequence of HBV DNA combined with recombinant HBV surface antigen
Tofacitinib/Pfizer	Rheumatoid arthritis	2/28/13, EMA. Tofacitinib is a small-molecule JAK-3, JAK-1 and JAK-2 inhibitor
Canagliflozin/J&J	Type II diabetes	3/29/13, PDUFA. Canagliflozin is a small-molecule sodium glucose cotransporter-2 inhibitor
Ponatinib/Ariad	Chronic myelogenous leukemia	3/27/13, PDUFA. Ponatinib is a small-molecule pan-kinase inhibitor of Bcr, FGFR, ABL Src, Flt3, Kit, Ret and PDGF receptor
Crofelemer/Salix	Gastroenterologic disorders	3/31/13, FDA PDUFA. Crofelemer is a small-molecule proanthocyanidin from the bark of the Amazonian Croton tree, with antisecretory effect on gut ion channels
Lomitapide/ Aegerion	Dyslipidemia/hypercholesterolemia	1/1/13, EMA. Lomitapide is a microsomal triglyceride transfer protein inhibitor, affecting LDL production in the liver and chylomicrons in the intestine
Scenesse (afamelanotide)/Clinuvel	Porphyria	1/1/13, EMA. Scenesse is a synthetic analog of the alpha-melanocyte–stimulating hormone, which binds to melanocortin receptor 1
Celltrion	Rheumatoid arthritis	2/1/13, EMA. Remsima is a biosimilar chimeric human-murine IgG1 mAb infliximab
Cobicistat/Gilead	HIV/AIDS	3/1/13, EMA. is a small-molecule CYP3A inhibitor to potentiate CYP3A metabolized antivirals
Vortioxentine/ H. Lundbeck	Major depressive disorder	1/31/13, EMA. (small-molecule 5-HT 3 and 5-HT 7 antagonist, 5-HT 1B partial agonist, 5AHT 1A agonist and 5-HT transporter inhibitor

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). PDUFA, Prescription Drug User Fee Act; J&J, Johnson & Johnson. LDL, low-density lipoprotein; FGFR, fibroblast growth factor receptor; PDGF, platelet-derived growth factor; mAb, monoclonal antibody.

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